REMARKS

Claims 1-4, 12-13 and 33-34 are pending. Applicants cancel non-elected claims without prejudice to future prosecution of that subject matter.

Double Patenting

Claims 1-4, 12-13, 26-28 and 33-34 were rejected under the judicially-created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 14 and 16 of U.S. Patent 5,753,491 (the '491 patent). Applicants traverse.

The statement in the final Office Action that "the instant claims recite open claim language, and further encompass immortal human multipotent CNS neural stem cells, as claimed in '491" (page 2) is irrelevant to establishing a case of prima facie obviousness because no evidence is cited in the Action that it would be obvious isolate cholera-toxin negative (ChTx-) multipotent cells (i.e., Applicants' claimed invention) from a neuro-glial cell line as claimed in the '491 patent. Lacking evidence that one of ordinary skill in the art would have been motivated at the time Applicants' invention was made to modify the cell lines of the '491 patent and to isolate multipotent cells as claimed in this application, no prima facie case of obviousness is proved.

The '491 patent does not teach that the multipotent cells utilized by Applicants and claimed here are cholera-toxin negative (ChTx-) cells. The allegation in the Action that the '491 patent's "multipotent neural stem cells inherently are ChTx negative" (page 3) is incorrect. Multipotent stem cells can be either cholera-toxin negative or cholera-toxin positive. Therefore, cholera-toxin negative (ChTx-) status is not an inherent characteristic of multipotent stem cells. "Inherency . . . may not be established by probabilities or possibilities." *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991), quoting *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (C.C.P.A. 1981). The burden is on the Patent Office to cite evidence that the allegedly inherent limitation is necessarily present in the prior art reference, not on Applicants to prove otherwise. *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950 (Fed. Cir. 1999).

Shindler et al. (Dev. Brain Res. 92:199-210, 1998) was cited on pages 2-3 of the Action because they allegedly "teach that only differentiating neurons bind to ChTx." To

the contrary, Shindler et al. actually teach that some of the cells that bind to cholera toxin will go on to become glial cells. GFAP is a marker for astrocytes, a type of glial cell. Table 1 of Shindler et al. (page 204) shows that approximately 2% of the cholera toxin (CTB)-labeled cells went on to become GFAP-positive (i.e., to display an astrocytic phenotype) at the 48-hour time point. Clearly, cells that go on to become astrocytic glial cells cannot have been differentiating neurons. Accordingly, not only do Shindler et al. not support the allegation in the Action that multipotent nervous system cells having the potential to differentiate toward a neuronal cell or a glial cell are inherently ChTx negative, but Shindler et al. is actually evidence that multipotent cells are not necessarily cholera-toxin negative. Therefore, cholera-toxin negative status is not an inherent characteristic of multipotent stem cells.

Withdrawal of the double patenting rejection is requested.

35 U.S.C. 102 – Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 1-4, 12-13, 26-28 and 33-34 were rejected under Section 102(e) as allegedly anticipated by Major et al. (U.S. Patent 5,753,491). Applicants traverse.

The statement in the final Office Action that "the instant claims recite open claim language, which therefore encompass Major's immortal human multipotent CNS neural stem cell line" (page 3) is irrelevant to establishing a case of prima facie obviousness because no evidence is cited in the Action that it would be obvious isolate cholera-toxin negative (ChTx-) multipotent cells (i.e., Applicants' claimed invention) from a neuro-glial cell line as claimed in the '491 patent. Here, Applicants' specification describes the selection of multipotent cells based on the lack of expression of the ChTx marker. In contradiction to the assertion in the Action that "similar methods" are used to generate the cells of the '491 patent and this application (page 3), Major et al. do not describe the method used by Applicants (e.g., selection of multipotent cells that are ChTx- or cell

sorting by flow cytometry) in the '491 patent. Lacking evidence that one of ordinary skill in the art would have been motivated at the time Applicants' invention was made to modify the cell lines of the '491 patent and to isolate multipotent cells as claimed in this application, no prima facie case of obviousness is proved.

The '491 patent does not teach that the multipotent cells utilized by Applicants and claimed here are cholera-toxin negative (ChTx-) cells. The allegation in the Action that the '491 patent's "multipotent neural stem cells are inherently ChTX negative, by definition" (page 3) is incorrect. Multipotent stem cells can be either cholera-toxin negative or cholera-toxin positive. Therefore, cholera-toxin negative (ChTx-) status is not an inherent characteristic of multipotent stem cells. "Inherency . . . may not be established by probabilities or possibilities." *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991), quoting *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (C.C.P.A. 1981). The burden is on the Patent Office to cite evidence that the allegedly inherent limitation is necessarily present in the prior art reference, not on Applicants to prove otherwise. *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950 (Fed. Cir. 1999).

Shindler et al. (Dev. Brain Res. 92:199-210, 1998) was cited on page 3 of the Action because they allegedly "teach that only differentiating neurons bind to ChTx." To the contrary, Shindler et al. actually teach that some of the cells that bind to cholera toxin will go on to become glial cells. GFAP is a marker for astrocytes, a type of glial cell. Table 1 of Shindler et al. (page 204) shows that approximately 2% of the cholera toxin (CTB)-labeled cells went on to become GFAP-positive (i.e., to display an astrocytic phenotype) at the 48-hour time point. Clearly, cells that go on to become astrocytic glial cells cannot have been differentiating neurons. Accordingly, not only do Shindler et al. not support the allegation in the Action that multipotent nervous system cells having the potential to differentiate toward a neuronal cell or a glial cell are inherently ChTx negative, but Shindler et al. is actually evidence that multipotent cells are not necessarily cholera-toxin negative. Therefore, cholera-toxin negative status is not an inherent characteristic of multipotent stem cells.

Claims 1-4, 12-13, 26-28 and 33-34 were rejected under Section 102(e) as allegedly anticipated by Weiss et al. (U.S. Patent 5,750,376). Applicants traverse.

The '376 patent does not teach that the multipotent cells utilized by Applicants and claimed here are cholera-toxin negative (ChTx-) cells. The allegation in the final Office Action that the '376 patent's "multipotent CNS neural stem cells/neurospheres are inherently ChTx negative, by definition" is incorrect. Multipotent stem cells can be either cholera-toxin negative or cholera-toxin positive. Therefore, cholera-toxin negative (ChTx-) status is not an inherent characteristic of multipotent stem cells. "Inherency . . . may not be established by probabilities or possibilities." *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991), quoting *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (C.C.P.A. 1981). The burden is on the Patent Office to cite evidence that the allegedly inherent limitation is necessarily present in the prior art reference, not on Applicants to prove otherwise. *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950 (Fed. Cir. 1999).

Shindler et al. (Dev. Brain Res. 92:199-210, 1998) was cited on page 4 of the Action because they allegedly "teach that only differentiating neurons bind to ChTx." To the contrary, Shindler et al. actually teach that some of the cells that bind to cholera toxin will go on to become glial cells. GFAP is a marker for astrocytes, a type of glial cell. Table 1 of Shindler et al. (page 204) shows that approximately 2% of the cholera toxin (CTB)-labeled cells went on to become GFAP-positive (i.e., to display an astrocytic phenotype) at the 48-hour time point. Clearly, cells that go on to become astrocytic glial cells cannot have been differentiating neurons. Accordingly, not only do Shindler et al. not support the allegation in the Action that multipotent nervous system cells having the potential to differentiate toward a neuronal cell or a glial cell are inherently ChTx negative, but Shindler et al. is actually evidence that multipotent cells are not necessarily cholera-toxin negative. Therefore, cholera-toxin negative status is not an inherent characteristic of multipotent stem cells.

Withdrawal of the Section 102 rejections is requested because all limitations of the claimed invention are not disclosed by the cited reference.

Conclusion

Having fully responded to all of the pending rejections, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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